

Walk, Roger A.

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Sent: Friday, January 10, 2003 1:00 PM
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Subject: Progress on Project with K.Janda and CS-induced AGEs

I appreciate the numerous responses regarding Kim Janda's proposal 'Nornicotine (NN) based aberrant protein glycation' and I would like to summarize progress over the past month. With regard to NN, the general consensus indicates that this is an interesting field of research but NN is present only at low levels in blood and it is probably not a major inducer of advanced glycosylation endproducts (AGEs). Although further experiments should be performed on this topic (e.g., determination of the levels of NN-AGEs in human smokers, etc.), it was suggested that a good avenue of funding would be the ERP. In December, I took the opportunity to set up a meeting with K.Janda in San Diego and we discussed on Dec. 23 the possibility of him submitting this proposal on NN to the ERP. Dr. Janda appeared to be interested in this possibility and he would like more information on the ERP. However, if NN is not the major AGE-inducing compound in cigarette smoke (CS), what are the major players in this process?

If we could generate tools that would identify those compounds in CS that induce the glycosylation of proteins, this information would be important for product development. Moreover, these tools could also be employed to develop assays for animal and clinical samples to document that our new products have a positive effect on a biological marker. Monoclonal antibodies (MABs) are powerful tools for research and product development in the pharmaceutical industry, and Janda's research has already shown that he can develop these tools against a compound in CS that induces AGE formation. Therefore, is it possible to utilize this technology to develop MABs against CS-induced AGEs and identify the key players in this process?

Although we could develop polyclonal antibodies against AGEs, we have little experience in the production of MABs and a contract or collaboration would be a relevant approach. Dr. Janda appears to be receptive to a collaboration regarding the generation and use of MABs to CS-induced AGEs, and we discussed the possibility of a small project. I agree that the overhead at Scripps is high with approximately 88% requested for a standard grant (e.g., federal grant). Unfortunately, Scripps subsequently imposes an additional 25% overhead cost for an industrial grant (I do not understand the rationale for the last item). I am looking at a way to reduce the impact of the total overhead for this project. Current information in the literature points to AGEs playing a major role in cardiovascular disease and it is known that AGEs are elevated in blood and tissues of smokers. I believe that internal communication of this project's goal is essential for us and my current strategy is to structure a project with K.Janda that can be used for discussion purposes and subsequently follow-up, perhaps during a tox meeting. Feedback on this strategy would be appreciated.

Ray Schleef